General

Guideline Title

Screening, monitoring, and treatment of stage 1 to 3 chronic kidney disease: a clinical practice guideline from the Clinical Guidelines Committee of the American College of Physicians.

Bibliographic Source(s)

Qaseem A, Hopkins RH, Sweet DE, Starkey M, Shekelle P. Screening, monitoring, and treatment of stage 1 to 3 chronic kidney disease: a clinical practice guideline from the Clinical Guidelines Committee of the American College of Physicians. Ann Intern Med. 2013 Dec 17;159(12):835-47. [106 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The strength of the evidence (high, moderate, low, or insufficient evidence to determine benefits or risks) and strength of recommendations (strong, weak) are defined at the end of the "Major Recommendations" field.

Recommendation 1: *The American College of Physicians (ACP) recommends against screening for chronic kidney disease (CKD) in asymptomatic adults without risk factors for CKD.* (Grade: weak recommendation; low-quality evidence)

Screening is recommended when it improves important clinical outcomes while limiting harms for screened individuals. Screening for CKD does not meet these generally accepted criteria for population-based screening. Although prevalence increases with age, CKD has a relatively low prevalence in the general population without risk factors. The accuracy of available screening measures for CKD or its progression is uncertain. No available evidence evaluates the sensitivity and specificity of various screening tests in the general population. Albuminuria and serum creatinine-derived estimated glomerular filtration rate (GFR) are widely available in primary care settings, with a high sensitivity and high specificity for 1-time measures of renal damage or dysfunction, but the risk for false-positive results is also very high.

There was no evidence evaluating the benefits of early treatment in patients identified by screening. In contrast, harms, including false-positive results, disease labeling, and unnecessary testing and treatment, are associated with the screening. Given the potential harms of screening for stage 1 to 3 CKD and unknown benefits, current evidence does not support screening for stage 1 to 3 CKD in adults without risk factors.

Recommendation 2: *ACP recommends against testing for proteinuria in adults with or without diabetes who are currently taking an*

angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II–receptor blocker (ARB). (Grade: weak recommendation; low-quality evidence)

Evidence suggests that treatment with ACE inhibitors (moderate-quality evidence) or ARBs (high-quality evidence) reduces the risk for end-stage renal disease (ESRD). Whether there are additional benefits of testing patients who are already taking ACE inhibitors or ARBs for proteinuria is unknown. Proteinuria is an intermediate marker; there is no evidence that monitoring proteinuria levels in patients taking ACE inhibitors or ARBs is beneficial or that reduced proteinuria levels translate into improved outcomes for patients with CKD.

Recommendation 3: *ACP recommends that clinicians select pharmacologic therapy that includes either an ACE inhibitor* (moderate-quality evidence) *or an ARB* (high-quality evidence) *in patients with hypertension and stage 1 to 3 chronic kidney disease.* (Grade: strong recommendation)

Evidence showed that treatment with ACE inhibitors (moderate-quality) or ARBs (high-quality) reduces the risk for ESRD in patients with stage 1 to 3 CKD. These medications also reduced composite renal outcomes, the risk for doubling of serum creatinine, and the progression from microalbuminuria to macroalbuminuria. Head-to-head trials revealed no difference in outcomes with ACE inhibitors or ARBs. The harms of ACE inhibitors include cough, angioedema, hyperkalemia, rash, loss of taste, and leukopenia. The harms of ARBs include hyperkalemia, angioedema, and dizziness.

The current evidence did not show any benefit of combination therapy with an ACE inhibitor plus an ARB compared with monotherapy with ACE inhibitors or ARBs. In addition, the risk for adverse effects significantly increased with ACE inhibitor plus ARB combination therapy, including cough, hyperkalemia, hypotension, and acute kidney failure requiring dialysis.

Evidence revealed no difference in ESRD or mortality between strict blood pressure control (128 to 133/75 to 81 mm Hg) and standard control (134 to 141/81 to 87 mm Hg).

Recommendation 4: *ACP recommends that clinicians choose statin therapy to manage elevated low-density lipoprotein in patients with stage 1 to 3 chronic kidney disease.* (Grade: strong recommendation; moderate-quality evidence)

High-quality evidence showed that statins reduced the risk for all-cause mortality. Evidence also showed that statins lower the risk for myocardial infarction (MI), stroke, and most cardiovascular outcomes in patients with stage 1 to 3 CKD. Patients included in the studies had mean low-density lipoprotein levels of 142 mg/dL (range, 109 to 192 mg/dL).

Two recently published systematic reviews not included in the Agency for Healthcare Research and Quality (AHRQ) report also showed benefits of lipid lowering therapy or statin therapy in patients with CKD. One study showed that statin therapy decreased mortality and cardiovascular events in patients with stage 1 to 3 CKD, and the other study showed that lipid-lowering therapy (including statins) decreased cardiac death and atherosclerosis-mediated cardiovascular events in patients with CKD. Low-quality evidence showed no effect on the risk for ESRD in patients with stage 1 to 3 CKD.

Definitions:

Grading of Quality of Evidence

High-Quality Evidence: Evidence is considered high quality when it is obtained from 1 or more well-designed and well-executed randomized, controlled trials (RCTs) that yield consistent and directly applicable results. This also means that further research is very unlikely to change confidence in the estimate of effect.

Moderate-Quality Evidence: Evidence is considered moderate quality when it is obtained from RCTs with important limitations—for example, biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity (even if it is generated from rigorous RCTs), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case–control analytic studies, and multiple time series with or without intervention are in this category. Moderate-quality evidence also means that further research will probably have an important effect on confidence in the estimate of effect and may change the estimate.

Low-Quality Evidence: Evidence obtained from observational studies would typically be rated as low quality because of the risk for bias. Low-quality evidence means that further research is very likely to have an important effect on confidence in the estimate of effect and will probably change the estimate. However, the quality of evidence may be rated as moderate or even high, depending on circumstances under which evidence is obtained from observational studies. Factors that may contribute to upgrading the quality of evidence include a large magnitude of the observed effect, a dose–response association, or the presence of an observed effect when all plausible confounders would decrease the observed effect.

Insufficient Evidence to Determine Net Benefits or Risks: When the evidence is insufficient to determine for or against routinely providing a service, the recommendation is graded as "insufficient evidence to determine net benefits or risks." Evidence may be conflicting, of poor quality, or lacking, and hence the balance of benefits and harms cannot be determined. Any estimate of effect that is very uncertain as evidence is either unavailable or does not permit a conclusion.

The American College of Physicians Guideline Grading System*		
Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced with Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

*Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Stage 1 to 3 chronic kidney disease (CKD)

Guideline Category

Management

Screening

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Nephrology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To present the evidence and provide clinical recommendations on the screening, monitoring, and treatment of adults with stage 1 to 3 chronic kidney disease (CKD)

Target Population

Adults with stage 1 to 3 chronic kidney disease (CKD)

Interventions and Practices Considered

1. Screening for chronic kidney disease based (CKD) on symptoms and risk factors
2. Testing for proteinuria
3. Angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II-receptor blocker (ARB)
4. Statin therapy

Major Outcomes Considered

- All-cause mortality
- Cardiovascular mortality
- Myocardial infarction
- Stroke
- Chronic heart failure
- Composite vascular outcomes
- Composite renal outcomes
- End-stage renal disease
- Quality of life
- Physical function
- Activities of daily living

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by the Minnesota Evidence-based Practice

Center (EPC), Minneapolis, MN for the Agency for Healthcare Research and Quality (AHRQ) (see the "Availability of Companion Documents" field).

Data Sources

The EPC staff searched MEDLINE to identify randomized, controlled trials (RCTs) published from 1985 to 25 November 2011. They manually reviewed reference lists of relevant articles and articles suggested by experts. For complete search strategies, see Appendix 1 of the systematic review (see the "Availability of Companion Documents" field).

Study Selection

The EPC staff applied separate eligibility criteria for chronic kidney disease (CKD) screening, monitoring, and treatment. Trained reviewers examined titles, abstracts, and full articles for eligibility. A second reviewer evaluated a 10% sample of abstracts. When discrepancies were identified, all abstracts initially reviewed by 1 reviewer were reviewed by a second reviewer. Randomized, controlled trials that included participants who at least approximated the definitions for CKD stages 1 to 3 were considered to be eligible for the questions about CKD monitoring and treatment. Only English-language studies were included.

Number of Source Documents

110 trials were included.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading of Quality of Evidence

High-Quality Evidence: Evidence is considered high quality when it is obtained from 1 or more well-designed and well-executed randomized, controlled trials (RCTs) that yield consistent and directly applicable results. This also means that further research is very unlikely to change confidence in the estimate of effect.

Moderate-Quality Evidence: Evidence is considered moderate quality when it is obtained from RCTs with important limitations—for example, biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity (even if it is generated from rigorous RCTs), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case–control analytic studies, and multiple time series with or without intervention are in this category. Moderate-quality evidence also means that further research will probably have an important effect on confidence in the estimate of effect and may change the estimate.

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Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by the Minnesota Evidence-based Practice Center (EPC), Minneapolis, MN for the Agency for Healthcare Research and Quality (AHRQ) (see the "Availability of Companion Documents" field).

Data Extraction and Quality Assessment

For each article, a first reviewer extracted details on study design, participant characteristics, outcomes, and adverse events and rated study quality. A second reviewer checked the extracted data for accuracy. A priori, the EPC staff selected mortality and end-stage renal disease (ESRD) as the primary efficacy outcomes, followed by clinical cardiovascular events (for example, myocardial infarction [MI], stroke, and congestive heart failure [CHF]), and composite vascular and renal outcomes that included these outcomes. Biochemical outcomes, such as halving of glomerular filtration rate (GFR), doubling of serum creatinine, and conversion from microalbuminuria to macroalbuminuria, were considered secondary and are reported in Supplements 1, 2, and 3. By using criteria developed by the Cochrane Collaboration, the authors rated individual RCT quality as good, fair, or poor on the basis of the adequacy of allocation concealment, blinding, reporting of reasons for attrition, and how analyses accounted for incomplete data. By using methods developed by the AHRQ and the Effective Health Care Program, the authors evaluated overall strength of evidence for mortality and ESRD outcomes for each treatment comparison on the basis of the criteria of risk for bias, consistency, directness, and precision. The EPC staff resolved discrepancies in quality and strength of evidence ratings by discussion and consensus.

Data Synthesis and Analysis

The EPC staff pooled results if clinical heterogeneity of patient populations, interventions, and outcomes was minimal. Data were analyzed in Review Manager 5.0 (Cochrane Collaboration, Oxford, United Kingdom). Random-effects models were used to generate pooled estimates of relative risks (RRs) and 95% CI. Statistical heterogeneity was summarized by using the I^2 statistic. When there were few randomized controlled trials (RCTs) for a given treatment and no overlap of reported outcomes, the EPC staff synthesized the data qualitatively.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

This guideline is based on a systematic evidence review sponsored by the Agency for Healthcare Research and Quality (AHRQ). Staff at the AHRQ and a technical expert panel, including members of the American College of Physicians Clinical Guidelines Committee and U.S. Preventive Services Task Force and others, helped to develop and refine the scope of this guideline that addressed the following key questions:

1. In asymptomatic adults with or without recognized risk factors for chronic kidney disease (CKD) incidence, progression, or complications, what direct evidence is there that systematic CKD screening improves clinical outcomes?
2. What harms result from systematic CKD screening in asymptomatic adults with or without recognized risk factors for CKD incidence, progression, or complications?
3. Among adults with CKD stages 1 to 3, whether detected by systematic screening or as part of routine care, what direct evidence is there that monitoring for worsening kidney function or kidney damage improves clinical outcomes?
4. Among adults with CKD stages 1 to 3, whether detected by systematic screening or as part of routine care, what harms result from monitoring for worsening kidney function or kidney damage?
5. Among adults with CKD stages 1 to 3, whether detected by systematic screening or as part of routine care, what direct evidence is there that treatment improves clinical outcomes?
6. Among adults with CKD stages 1 to 3, whether detected by systematic screening or as part of routine care, what harms result from treatment?

Rating Scheme for the Strength of the Recommendations

The American College of Physicians Guideline Grading System*		
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	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced with Risks and Burden
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Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

*Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group.

Cost Analysis

Published cost analyses were reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was approved by the American College of Physicians (ACP) Board of Regents on 17 November 2012.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

See the "Benefits" sections in the original guideline document for specific benefits (derived from both direct and indirect evidence) of screening and monitoring for chronic kidney disease (CKD).

Potential Harms

See the "Harms" sections in the original guideline document for specific harms (derived from both direct and indirect evidence) of screening, monitoring, and treatment for chronic kidney disease (CKD).

Qualifying Statements

Qualifying Statements

- Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment.
- The authors of this article are responsible for its contents, including any clinical or treatment recommendations. No statement in this article should be construed as an official position of the U.S. Department of Veterans Affairs.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

Patient Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Qaseem A, Hopkins RH, Sweet DE, Starkey M, Shekelle P. Screening, monitoring, and treatment of stage 1 to 3 chronic kidney disease: a clinical practice guideline from the Clinical Guidelines Committee of the American College of Physicians. Ann Intern Med. 2013 Dec 17;159(12):835-47. [106 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Dec 17

Guideline Developer(s)

American College of Physicians - Medical Specialty Society

Source(s) of Funding

Financial support for the development of this guideline comes exclusively from the American College of Physicians (ACP) operating budget.

Guideline Committee

Clinical Guidelines Committee of the American College of Physicians

Composition of Group That Authored the Guideline

Authors: Amir Qaseem, MD, PhD, MHA; Robert H. Hopkins Jr., MD; Donna E. Sweet, MD; Melissa Starkey, PhD; and Paul Shekelle, MD, PhD

Clinical Guidelines Committee of the American College of Physicians: Paul Shekelle, MD, PhD (*Chair*); Roger Chou, MD; Molly Cooke, MD; Paul Dallas, MD; Thomas D. Denberg, MD, PhD; Nick Fitterman, MD; Mary Ann Forciea, MD; Robert H. Hopkins Jr., MD; Linda L. Humphrey, MD, MPH; Tanveer P. Mir, MD; Douglas K. Owens, MD, MS; Holger J. Schünemann, MD, PhD; Donna E. Sweet, MD; and Timothy Wilt, MD, MPH

Financial Disclosures/Conflicts of Interest

Dr. Shekelle: *Personal fees*: ECRI Institute, Veterans Affairs, UpToDate; *Grants:* Agency for Healthcare Research and Quality, Veterans Affairs, Centers for Medicare & Medicaid Services, Office of the National Coordinator for Health Information Technology. All other authors have no disclosures.

Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-3186 . A record of conflicts of interest is kept for each Clinical Guidelines Committee meeting and conference call and can be viewed at www.acponline.org/clinical_information/guidelines/guidelines/conflicts_cgc.htm .

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the Annals of Internal Medicine Web site .

Print copies: Available from the American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA 19106-1572.

Availability of Companion Documents

The following are available:

- Qaseem A, Snow V, Owens DK, Shekelle P. The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. Ann Intern Med. 2010 Aug 3;153(3):194-199. Electronic copies: Available from the Annals of Internal Medicine Web site.
- Fink H, Ishani A, Taylor BC, Green NL, MacDonald R, Rossini D, Sadiq S, Lankireddy S, Kane RL, Wilt TJ. Screening for, monitoring, and treatment of chronic kidney disease stages 1 to 3: a systematic review for the U.S. Preventive Services Task Force and for an American College of Physicians Clinical Practice Guideline. Ann Intern Med. 2012;156(8):570-81. Electronic copies: Available from the Annals of Internal Medicine Web site.
- Screening, monitoring, and treatment of stage 1 to 3 chronic kidney disease. Continuing Medical Education. Available from the Annals of Internal Medicine Web site.

Print copies: Available from the American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA 19106-1572.

A collection of Recommendation Summaries for all current American College of Physicians Clinical Guidelines is now available for download to mobile devices from the American College of Physicians Web site.

Patient Resources

The following is available:

- Summaries for patients. Screening, monitoring, and treatment of stage 1 to 3 chronic kidney disease: a clinical practice guideline from the American College of Physicians. Electronic copies: Available from the Annals of Internal Medicine Web site.

Print copies: Available from the American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA 19106-1572.

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NGC Status

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